

## **AMENDMENTS TO THE CLAIMS**

Claims 1 – 44 cancelled

45. (Currently Amended) A low-volume hybridization device, comprising:  
a base,

a pressure chamber,

a reaction chamber disposed in said base, said reaction chamber being bound by a flexible diaphragm separating said pressure chamber from said reaction chamber, and

a probe array mounted to said base and disposed over a surface inside said reaction chamber for hybridization, said flexible diaphragm being disposed over said surface of said array said pressure chamber and said flexible diaphragm being constructed to change a volume of said reaction chamber by application of pressure or vacuum to displace fluid in said reaction chamber over said surface of said array and thereby facilitate said hybridization.

46. (Previously presented) The low-volume hybridization device of claim 45, wherein said reaction chamber has a volume in the range of 0.1 to 100  $\mu$ l.

47. (Previously presented) The low-volume hybridization device of claim 45, wherein said reaction chamber has a volume in the range of 1 to 20  $\mu$ l.

48. (Previously Presented) The low-volume hybridization device of claim 45, further comprising:

a pneumatic system for providing said pressure or vacuum to said pressure chamber and thereby moving said flexible diaphragm.

Claims 49 – 65 cancelled

66. (Previously Presented) The low-volume hybridization device of claim 45 including an addressable heater thermally coupled to said reaction chamber.

67. (Previously Presented) The low-volume hybridization device of claim 66 including a thermal insulation in contact with said heater.

68. (Previously Presented) The low-volume hybridization device of claim 66 including a temperature sensor positioned adjacent said heater.

69. (Previously Presented) The low-volume hybridization device of claim 45, including a cooler thermally coupled to said reaction chamber.

70. (Previously Presented) The low-volume hybridization device of claim 69, wherein said cooler is a thermoelectric cooler.

71. (Previously Presented) The low-volume hybridization device of claim 45 further including an extraction chamber constructed and arranged to exchange fluids with said reaction chamber.

72. (Previously Presented) The low-volume hybridization device of claim 71, wherein said extraction chamber includes a porous flow-through plug having nucleic acid binding properties.

73. (Previously Presented) The low-volume hybridization device of claim 72, wherein said plug is a deformable plug.

74. (Previously Presented) The low-volume hybridization device of claim 45 wherein said device is constructed to introduce bubbles into said reaction chamber to provide for mixing at said array surface to enable fluid displacement over said array surface in said reaction chamber for achieving hybridization.

75. (Previously Presented) The low-volume hybridization device of claim 72, wherein said plug comprises glass wool.

76. (Previously Presented) The low-volume hybridization device of claim 72, wherein said plug is pretreated with an agent for enhancing the nucleic acid binding properties.

77. (Previously Presented) The low-volume hybridization device of claim 76, wherein said agent is selected from the group consisting of acids, bases, silanes, polysine, tethered antibodies, synthesized nucleic acids, and Poly-T DNA.

78. (Previously Presented) The low-volume hybridization device of claim 71, wherein said extraction chamber includes a textured surface having nucleic acid binding properties.

79. (Previously Presented) The low-volume hybridization device of claim 71, wherein said extraction chamber includes a structure comprising an open cell foam.

80. (Previously Presented) The low-volume hybridization device of claim 71, wherein said extraction chamber includes an affinity surface having particles attached thereto, the particles having nucleic acid binding properties.

81. (Previously Presented) The low-volume hybridization device of claim 80, wherein said affinity surface includes controlled-pore glass structures.

82. (Previously Presented) The low-volume hybridization device of claim 80, wherein said affinity surface has glass spheres attached thereto.

83. (Previously Presented) The low-volume hybridization device of claim 80, wherein said affinity surface has cellulose particles attached thereto.

84. (Previously Presented) The low-volume hybridization device of claim 80, wherein said affinity surface is microfabricated.

85. (Previously Presented) The low-volume hybridization device of claim 80, wherein said affinity surface is machined.

86. (Previously Presented) The low-volume hybridization device of claim 80, wherein said affinity surface is injection molded.

87. (Previously Presented) The low-volume hybridization device of claim 45 further including a base-unit including a manifold constructed and arranged to control said flexible diaphragm.

88. (Previously Presented) The low-volume hybridization device of claim 87 wherein said manifold is a vacuum manifold.

89. (Previously Presented) The low-volume hybridization device of claim 87 wherein said base-unit further includes flow connectors for delivering fluid to said reaction chamber.

90. (Previously Presented) The low-volume hybridization device of claim 87 wherein said base-unit further includes electrical connectors for controlling operation within said device.

91. (Previously Presented) A low-volume hybridization device, comprising:  
a base,  
a pressure chamber,  
a reaction chamber disposed in said base, said reaction chamber being bound by a flexible diaphragm separating said pressure chamber from said reaction chamber,  
a probe array mounted to said base and disposed over a surface inside said reaction chamber for hybridization, said flexible diaphragm forming an opposing surface to said surface of said array, said pressure chamber being constructed for application of pressure or vacuum to said flexible diaphragm and thereby changing a distance

between said array surface and said diaphragm surface to enable fluid displacement in said reaction chamber for achieving hybridization, and

a processing chamber connectable to said reaction chamber and constructed for exchanging fluids with said reaction chamber.

92. (Previously Presented) The low-volume hybridization device of claim 91 including a pneumatic manifold constructed and arranged to provide pressure or vacuum to said pressure chamber to displace said flexible diaphragm.

93. (Previously Presented) The low-volume hybridization device of claim 92 wherein said processing chamber includes an amplification chamber.

94. (Previously Presented) The low-volume hybridization device of claim 93 wherein said amplification chamber is constructed for PCR amplification.

95. (Previously Presented) The low-volume hybridization device of claim 92 wherein said processing chamber includes a sample acquisition chamber.

96. (Previously Presented) The low-volume hybridization device of claim 92 wherein said processing chamber includes an extraction chamber.

97. (Previously Presented) The low-volume hybridization device of claim 96, wherein said extraction chamber includes a porous flow-through plug having nucleic acid binding properties.

98. (Previously Presented) The low-volume hybridization device of claim 97, wherein said plug is a deformable plug.

99. (Previously Presented) The low-volume hybridization device of claim 45 wherein said device is constructed to introduce bubbles into said reaction chamber to

provide for mixing at said array surface to enable fluid displacement over said array surface in said reaction chamber for achieving hybridization.

100. (Previously Presented) The low-volume hybridization device of claim 97, wherein said plug comprises glass wool.

101. (Previously Presented) The low-volume hybridization device of claim 97, wherein said plug is pretreated with an agent for enhancing the nucleic acid binding properties.

102. (Previously Presented) The low-volume hybridization device of claim 96, wherein said extraction chamber includes a textured surface having nucleic acid binding properties.

103. (Previously Presented) The low-volume hybridization device of claim 96, wherein said extraction chamber includes a structure comprising an open cell foam.

104. (Previously Presented) The low-volume hybridization device of claim 96, wherein said extraction chamber includes an affinity surface having particles attached thereto, the particles having nucleic acid binding properties.

105. (Previously Presented) The low-volume hybridization device of claim 104, wherein said affinity surface includes controlled-pore glass structures.

106. (Previously Presented) The low-volume hybridization device of claim 104, wherein said affinity surface has glass spheres attached thereto.

107. (Previously Presented) The low-volume hybridization device of claim 104, wherein said affinity surface has cellulose particles attached thereto.

108. (Previously Presented) The low-volume hybridization device of claim 104, wherein said affinity surface is microfabricated.

109. (Previously Presented) The low-volume hybridization device of claim 104, wherein said affinity surface is machined.

110. (Previously Presented) The low-volume hybridization device of claim 104, wherein said affinity surface is injection molded.

111. (Previously Presented) A low-volume hybridization device, comprising:  
a base,

a pressure chamber including a pneumatic port,

a reaction chamber disposed in said base and including a fluidic port,

a probe array mounted to said base and disposed over a surface inside said reaction chamber, and

a flexible diaphragm disposed to separate said pressure chamber from said reaction chamber, said pressure chamber being constructed for application of pressure or vacuum to said flexible diaphragm using said pneumatic port to change a volume of said reaction chamber, and said device being constructed to introduce bubbles into said reaction chamber to provide for mixing at said array surface to enable fluid displacement in said reaction chamber for achieving hybridization.

112. (Previously Presented) The low-volume hybridization device of claim 111, wherein said reaction chamber has a volume in the range of 0.1 to 100  $\mu\text{l}$ .

113. (Previously Presented) The low-volume hybridization device of claim 111, wherein said reaction chamber has a volume in the range of 1 to 20  $\mu\text{l}$ .

114 (Previously Presented) The low-volume hybridization device of claim 111, further comprising:

a pneumatic system for providing said pressure or vacuum to said pressure chamber and thereby moving said flexible diaphragm.